

<p align="center"><b>Notice of Allowability</b></p>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/564,854	GUGLIELMOTTI ET AL.	
	<b>Examiner</b>  UMAMAHESWARI RAMACHANDRAN	<b>Art Unit</b>  1617	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--**

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 4/1/2009.
2. ☒ The allowed claim(s) is/are 1-7 and 9-16 and renumbered as 1-15.
3. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) ☒ All    b) ☐ Some\*    c) ☐ None    of the:
  1. ☒ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\* Certified copies not received: \_\_\_\_\_.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

**THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
  5. ☐ CORRECTED DRAWINGS ( as "replacement sheets") must be submitted.
    - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review ( PTO-948) attached
      - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date \_\_\_\_\_.
    - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date \_\_\_\_\_.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

**Attachment(s)**

- |   |  |
|---|--|
| <ol style="list-style-type: none"> <li>1. <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)</li> <li>2. <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948)</li> <li>3. <input checked="" type="checkbox"/> Information Disclosure Statements (PTO/SB/08),<br/>Paper No./Mail Date <u>3/30/2009</u></li> <li>4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit<br/>of Biological Material</li> </ol> | <ol style="list-style-type: none"> <li>5. <input type="checkbox"/> Notice of Informal Patent Application</li> <li>6. <input checked="" type="checkbox"/> Interview Summary (PTO-413),<br/>Paper No./Mail Date _____.</li> <li>7. <input checked="" type="checkbox"/> Examiner's Amendment/Comment</li> <li>8. <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance</li> <li>9. <input type="checkbox"/> Other _____.</li> </ol> |
|---|--|

### **EXAMINER'S AMENDMENT**

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Attorney, Thomas Cunningham on July 14 2009, July 23 2009.

The application has been amended as follows:

Please **INSERT** the following titles and descriptions at page 6, line 9.

### **BRIEF DESCRIPTION OF THE DRAWINGS**

Fig. 1. Effect on sciatic nerve ligature. The pain thresholds of rats treated with compound (I) and control rats were compared. 8 rats/group, mean " SEM; \*p < 0.05 vs. control, ANOVA followed by Dunnett's test. Pain threshold of normal animals of equal weight/age = 35.4 " 3.22 g.

Fig. 2. Effect on diabetic neuropathy. The pain thresholds of rats treated with compound (I) and control rats were compared. 8 rats/group, mean " SEM; \*p < 0.05 vs. control, ANOVA followed by Dunnett's test. Pain threshold of normal animals of equal weight/age = 252.5 " 6.20 g.

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- 1) In claim 1, line 2, After "administering" **DELETE** "to a subject having neuropathic pain" and **INSERT** – "to a human subject having neuropathic pain, 0.001 to 100 mg/kg/day of" --
- 2) In claim 1, line 12, After "inorganic acid" **DELETE** " , to prepare a pharmaceutical composition active in the treatment of neuropathic pain"
- 3) **DELETE** Claim 8
- 4) In claim 9, line 1, After "wherein" **DELETE** "said subject" and **INSERT** "the"
- 5) In claim 9. line 1, After "human" **DELETE** "and"
- 6) In claim 10, line 1, After "wherein" **DELETE** "said subject" and **INSERT** "the"
- 7) In claim 10. line 1, After "human" **DELETE** "and"
- 8) In claim 11, line 1, After "wherein" **DELETE** "said subject" and **INSERT** "the"
- 9) In claim 11. line 1, After "human" **DELETE** "and"
- 10) In claim 12, line 1, After "wherein" **DELETE** "said subject" and **INSERT** "the"
- 11) In claim 12. line 1, After "human" **DELETE** "and"
- 12) In claim 13, line 1, After "wherein" **DELETE** "said subject" and **INSERT** "the"
- 13) In claim 13. line 1, After "human" **DELETE** "and"
- 14) In claim 14, line 1, After "wherein" **DELETE** "said subject" and **INSERT** "the"
- 15) In claim 14. line 1, After "human" **DELETE** "and"
- 16) In claim 15, line 1, After "wherein" **DELETE** "said subject" and **INSERT** "the"
- 17) In claim 15. line 1, After "human" **DELETE** "and"
- 18) In claim 16, line 1, After "wherein" **DELETE** "said subject" and **INSERT** "the"
- 19) In claim 16. line 1, After "human" **DELETE** "and"

Claims 1-7, 9-16 are allowable and are renumbered as 1-15.

#### **DETAILED ACTION**

##### ***Status of Claims***

The examiner notes the receipt of the amendments and remarks received in the office on 3/20/2009 amending claims 1-3 and adding new claims 4-16. Claims 1-7, 9-16 are pending and are found allowable for the reasons given below.

##### ***Application Priority***

This application is a 371 of PCT/EP04/07635, 07/08/2004 and claims priority of ITALY, MI2003A 001468, 7/18/2003.

#### **REASONS FOR ALLOWANCE**

Claims 1- 3 rejected under 35 U.S.C. 101, 35 U.S.C. 112 are withdrawn due to the amendment of claims 1-3. Applicants' arguments regarding the rejection of claims 1-

3 under 35 U.S.C. 103(a) as being unpatentable over King et al. (Applicant cited IDS: WO 93/03725) in view of Uchida et al. (U.S. 6,624,162) have been found to be persuasive. Claims 1-7, 9-16 are allowable for the following reasons.

Claims 1-7, 9-16 are directed to a method of treating neuropathic pain comprising administering to a human the compound of formula I, in an amount of 0.001 to 100 mg/kg/day. The closest prior art of record are King, et al, WO93/03725 in view of Uchida, et al., U.S. Patent No. 6,624,162. King is cited as disclosing compounds of formula (I) on page 2 and the reference discloses a large genus of compounds of the formula: X-CO-Y-Z. The compound of formula (I) falls within the genus of King et al. and the substituents have to be selected to arrive at the instantly claimed compounds. Also, King et al. does not teach the compounds to be useful in treating pain. King does not disclose or suggest using a compound of X-CO-Y-Z to treat neuropathic pain, but this class of compounds exhibits antagonism for 5-HT<sub>4</sub> receptors which potentially might be used to treat IBS, atrial arrhythmias and stroke (page 2 of King et al.). Uchida et al. does not disclose the compounds of formula (I) of the invention, but has been applied as a secondary reference disclosing that 5-HT<sub>4</sub> modulators (agonists or antagonists) for treatment of pain. However, neither Uchida nor King disclose or suggest using compounds of formula (I) to treat neuropathic pain, nor even that 5-HT<sub>4</sub> antagonists reduce neuropathic pain. Therefore, these references could not have provided a reasonable expectation of success for treating a human exhibiting neuropathic pain using a 5-HT<sub>4</sub> antagonist, or selecting a compound of formula (I) for this purpose. Therefore, there is no anticipation or motivation of treating neuropathic pain comprising

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administering to a human the compound of formula I, in an amount of 0.001 to 100 mg/kg/day from the teaching or suggestion from prior art.

The claims are allowable over the closest art of record because they do not teach, disclose nor make obvious the claimed method of treating neuropathic pain comprising administering to a human the compound of formula I, in an amount of 0.001 to 100 mg/kg/day.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Umamaheswari Ramachandran whose telephone number is 571-272-9926. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1617